

C1  
Cont.  
d.) utilizing [the] said model of step c) to predict the response of said patient to  
[said] the selected treatment.

C2  
2. (amended) The method according to claim [2] 1, wherein said model is a multilayer  
neural network, and wherein said at least one automated non-linear algorithm is a  
back propagation learning algorithm.

C3  
6. (amended) The method according to claim 5, further comprising estimating said  
interactions between said predictive symptoms by multiplying [symptom  
severities] at least a first measured severity for a first predictive symptom times a  
second measured severity for a second predictive symptom.

C4  
7. (amended) The method according to claim 1, further comprising utilizing the model of  
step c) to rank [by response influence] the response to the treatment of at least  
one pre-treatment clinical symptom [predictive symptoms] to indicate the  
predictive importance of [a predictive] said at least one pre-treatment clinical  
symptom.

C5  
9. (amended) The method according to claim 1, wherein said [set of] predictive  
symptoms [comprises a plurality of:] are selected from the group consisting of  
Mood, Work, and Energy.

C5  
10.  
12. (amended) The method according to claim 1, wherein said [set of] predictive  
symptoms [comprises a plurality of:] are selected from the group consisting of  
Mood, Overall Severity, and Middle and Late Sleep.

C6  
12.  
15. (amended) A method of treating depression in a clinical patient comprising the  
following steps:

- C6  
cont.
- a.) defining a set of predictor variables which define a set of data of a baseline patient profile, said set of predictor variables comprising predictive symptoms and a set of treatment options;
  - b.) developing [an] a trained outcome prediction and an expected response for each treatment option of said set of treatment options, each said trained outcome prediction based upon an automated non-linear analysis of patient symptoms measured in at least one study over time in response to each said treatment option;
  - c.) selecting a first preferred treatment [option] from said set of treatment options based on said trained outcome prediction;
  - d.) applying said first preferred treatment [option] to said clinical patient to obtain a first response; and
  - e.) monitoring said patient by comparing [a] said first response of said clinical patient [to said treatment option] to said trained outcome prediction for said first preferred treatment to obtain a difference measurement which is used to provide an updated outcome prediction for said clinical patient.

13.  
16. (amended) The method of claim ~~15~~ <sup>12</sup> further including the step of selecting a second preferred treatment [option] from said set of treatment options based on said updated outcome prediction when said first response deviates from said trained outcome prediction for said first selected treatment.

- C7
14.  
36. (amended) A method of treating a disorder which is diagnosable and treated based upon a patient's symptom and for which a patient could have a variable response to treatment, comprising:

- a.) developing an outcome prediction for a set of treatment options and an integrated expected recovery pattern for each treatment option in said set of treatment options, said outcome prediction and said integrated expected recovery
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pattern for each said treatment option based on [an] computer analysis that utilizes a non-linear algorithm of known patient symptoms and recovery patterns;

b.) selecting for said patient a first preferred treatment option from said set of treatment options;

c.) generating a first expected recovery pattern associated with said first preferred treatment option, said first expected recovery pattern having a first expected recovery time period;

d.) applying said first preferred treatment option to said patient;

e.) monitoring said patient during said first expected recovery time period to develop a patient treatment response;

f.) comparing said patient treatment response and said first expected recovery pattern; and

g.) selecting a second preferred treatment option from said set of treatment options when said patient treatment response varies significantly from said first expected recovery pattern thereby defining a treatment intervention for said patient.

15.

~~37.~~ (amended) The method according to claim ~~36~~, wherein the monitoring of step e.)

comprises developing an individual patient recovery profile, and the comparing of step f.) and the selecting of step g.) comprise:

[a] 1.) developing a difference between said individual patient recovery profile and said first expected recovery pattern;

[b] 2.) determining whether said difference is within an acceptable range, indicating a normal patient recovery;

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- C7 Cont.
- [c] 3.) determining whether said difference is outside said acceptable range, indicating an unacceptable patient recovery pattern; and
  - [d] 4.) selecting a second preferred treatment option from said set of treatment options when said difference is outside said acceptable range.

18.

42. (amended) The method according to claim [36] <sup>26 141</sup> ~~41~~, wherein said treatment intervention effect is represented by an immediate effect and a delayed effect,

C8

said immediate effect represented by a step function, which step function coincides with the onset of treatment;

said delayed effect represented by a sigmoid function of time with delay and steepness of the onset of the delayed effect.

19.

60. (amended) A method for predicting a response of a patient to a treatment [of] for an affective disorder from at least one pre-treatment clinical symptom, comprising the steps of:

- C9
- a.) performing at least one measurement of said pre-treatment clinical symptom on said patient, said pre-treatment symptom being a predictive symptom, and measuring said pre-treatment clinical symptom at selected time intervals so as to derive data representing a baseline patient profile;
  - b.) defining a set of a plurality of predictor variables which define [a set of] data of said baseline patient profile, said set of predictor variables comprising predictive symptoms and a set of treatment options;
  - c.) deriving a model that represents a relationship between said set of predictor variables and [said] a response exhibited by a recipient of one of said set of treatment options [and said set of predictor variables], said relationship derived by using at least one automated non-linear algorithm; and
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C9  
cont

d.) utilizing said model of step c) to predict the response of said patient to said treatment by comparing said model and said baseline patient profile.

C10

24.  
60. (amended) The method according to claim <sup>23</sup>60, further comprising estimating said interactions between said predictive symptoms by multiplying [symptom severities] at least a first measured severity for a first predictive symptom times a second measured severity for a second predictive symptom.

C11

25.  
60. (amended) The method according to claim <sup>19</sup>60, further comprising utilizing the model of step c) to rank by [response influence] influence on the response each of said predictive symptoms to indicate the predictive importance of [a] each of said predictive [symptom] symptoms and utilizing the predictive importance to select of at least one of said predictive symptoms for use in measuring said pre-treatment clinical symptom.

26.  
70. (amended) The method according to claim <sup>19</sup>60, wherein said set of predictive symptoms [comprises a plurality of:] is selected from the group consisting of Mood, Work, and Energy.

C12

28.  
71. (amended) The method according to claim <sup>19</sup>60, wherein said set of predictive symptoms [comprises a plurality of:] is selected from the group consisting of Mood, Severity, and Middle and Late Sleep.

29.  
72. (amended) The method according to claim <sup>19</sup>60, further comprising: before step a), providing at least one paired set of a known baseline patient [profiles] profile and a treatment [outcomes] outcome, which [known profiles and outcomes are] at least one paired set is used in step c) for deriving said model.

C13

31.  
74. (amended) A method of treating an affective disorder in a patient comprising the following steps:

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- C13  
Cont.
- a.) defining a set of predictor variables [which define], said set of predictor variables defining a set of data of a baseline patient profile, said set of predictor variables comprising predictive symptoms and a set of treatment options;
  - b.) developing an outcome prediction for said set of treatment options, said outcome prediction based upon an analysis of patient symptoms, said analysis utilizing an automated nonlinear algorithm;
  - c.) selecting a first preferred treatment option from said set of treatment options based on said outcome prediction;
  - d.) applying said first preferred treatment option to said patient; and
  - e.) monitoring said patient by comparing a response of said patient to said treatment option to said outcome prediction to provide an updated outcome prediction for said patient.

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#### RESPONSE

Claims 1-16, 36-38, 42, 44, and 60-75 stand rejected. Claims 2, 8, 13, 61 and 67 have been canceled. Claims 1, 7, 9, 11, 12, 15, 36, 37, 60, 66, 68, 70, 71, 72, and 74 have been amended. No new matter is believed to have been added. Amendments find support in the Specification. Claims 1, 3-7, 9-12, 14-16, 36-38, 42, 44, 60, and 62-66, 68-75 remain. Independent claims have been clarified to indicate that the methods use a model or an analysis that requires a computerized or automated non-linear algorithm. Further, the claims have been clarified to indicate that the model or analysis is developed using data accumulated from patients other than the patient currently seeking treatment. However, this is not meant to preclude use of the data collected from the patient seeking treatment for subsequent incorporation into the model or analysis. Treatment predictions or choices for the clinical patient are then made based upon comparison of the patient data with expected data obtained from analysis and modeling of data obtained from patients who have previously been studied

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1.-2. The Examiner has rejected claims 1-16, 36-38, 42, 44, and 60-75 under 35 U.S.C. 112, second paragraph stating that these claims are indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicant regards as the invention. Claims 2, 8, 13, 61, and 67 have been canceled. Claims 1, 7, 9, 11, 12, 15, 37, 42, 60, 66, 68, 70, 71, 72, and 74 have been amended based upon the Examiner's helpful suggestions.

The Applicant respectfully requests that the Examiner withdraw his rejections and objections and allow all remaining claims.

3.-4. The Examiner has rejected claims 1-16, 36-38, 42, 44, and 60-75 under 35 U.S.C. 102 (b) as being clearly anticipated by Chapter 4 of the Luciano dissertation. Accompanying this Response is a Declaration by Joanne Sylvia Luciano, the above named Applicant, stating that she is the author of Chapter 4, that the Dissertation including Chapter 4 which forms the basis for the provisional application filing did not become publicly available until about June, 1996, which is less than one year before applying for US patent as US Provisional Application 60/041,287 filed March 20, 1997 from which the above identified Application claims priority. Thus, Chapter 4 is not available as a reference.

The Applicant respectfully requests that the Examiner withdraw his rejections and allow all claims.

5. The Examiner has rejected claims 1, 8, 9, 13, 60, 64, 65, 67, 68, and 72 under 35 U.S.C. 102(b) as being anticipated by Parker et. al. in "Predicting Improvement in Patients..." Claims 8 and 67 have been canceled. The Examiner states that Parker et. al. discuss results of a study of patients with non-endogenous depression which includes defining values and performing analyses to allow prediction of outcome in patients receiving psychiatric assessment and therapy (particularly Results and Discussion). The Examiner suggests that Parker et al. state that the analyses were used to assess the relevance of baseline variables as predictors of improvements for psychotherapy or counseling.



The present invention facilitates selection by the clinician of the most advantageous treatment for the individual patient. Parker et al. serves merely to identify subjective predictors such as break-up of an intimate relationship rather than using standardized measurements, such as the Hamilton Instrument or standardized test values such as a blood sample value of a relevant biochemical, for assessment. Further in one aspect, unlike Parker et al., the present invention is directed to a method for predicting a response to a treatment of a disorder, be it depression or other disorder, where multiple treatment options are available and the patient can demonstrate variable outcome to treatment. The present invention utilizes a model, that provides a relationship that is obtained using a computerized non-linear algorithm between a response to treatment and a set of identified predictor variables. The predictor variables are derived from predictive symptoms and treatment options taken together. Parker et al. does not state how their processing is implemented.

For these reasons, the Applicant respectfully requests that the Examiner withdraw his rejections and allow all claims.

6. The Examiner has rejected claims 15, 16, 36-38, 42, 44, 74, and 75 under 35 U.S.C. 102(b) as being anticipated by the method used by a doctor in treating a patient. The claims have been amended to clarify that the above identified invention uses a non-linear algorithm for data analysis.

The Applicant respectfully requests that the Examiner provide support for his assertion that a doctor uses the method in the claims that have been rejected for treating a patient exhibiting an affective disorder or depression. Brill in US Patent No. 5,435,324 notes (at col. 1, lines 45-67) the difficulty assessing providing a patient with beneficial treatment experienced by even the seasoned psychotherapy provider.

Further, Patterson notes the difficulties encountered by clinicians and the difficulty inherent in computerizing diagnosis of treatment and recovery predictions. Notably in the present invention, the modeling and analysis are objective and guidance is provided regarding the particular parameters and their use in computerized or automated algorithms that are useful for analysis and prediction of treatment and recovery. It is



known that even experts make errors in judgement based upon 1.) sample size effects ie. Clinicians base their judgements on patients they have treated; 2.) a tendency to remember positive responses over negative responses and to therefore give preference to treatments they have had success with rather than considering all possible treatments; 3.) depending too much on ease of recall; and 4.) anchoring errors which are exemplified by estimating commercial plane deaths from auto deaths vs. train deaths (Patterson, Robert; "Clinical Applications of Computerized Algorithms", <http://www.mhc.com/algorithm.html> - enclosed). Thus it is critical that the subjectivity of human judgement be reduced when assigning and assessing treatment for diseases and maladies that are difficult to diagnose and for which there are several treatments which at first blush may appear to affect relief from symptoms.

For these reasons, the Applicant respectfully requests that the Examiner withdraw his rejections and allow all claims.

7.-8. The Examiner has rejected claims 2, 11, 12, 61, 70, and 71 under 35 U.S.C. 103(a) as being unpatentable over Parker, et. al. Claim 2 has been cancelled. The rejected claims have been amended through the amendment of the independent claim upon which they depend to include the limitation that the model in the independent claims upon which these claims are dependent is an automated non-linear model. Parker does not use or recognize that an automated non-linear algorithm is useful to provide a predictive model.

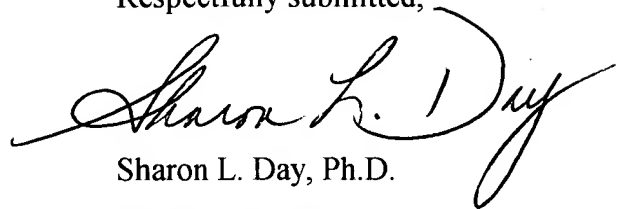
For this reason, the Applicant respectfully requests that the Examiner withdraw his rejections and allow all claims.

9. The Applicant thanks the Examiner for pointing out Beekman et al. and Brill which were not relied upon.

The Applicant thanks the Examiner for his helpful suggestions and respectfully requests that the Examiner withdraw his rejections and allow all claims, submitting that the above identified application is in condition for allowance.

Should the Examiner have any questions or suggestions, please contact the Applicant's Agent at either of the telephone numbers given below.

Respectfully submitted,

A handwritten signature in cursive script that reads "Sharon L. Day". The signature is written in black ink and is positioned above the printed name.

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